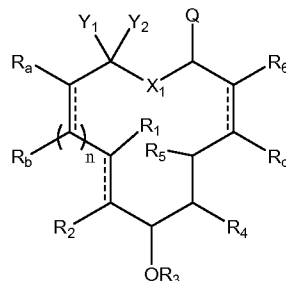


AMENDMENTS TO THE CLAIMS

The following **Listing of Claims** will replace all prior versions, and listings of claims in the application.

1. **(CURRENTLY AMENDED)** A compound having the structure:

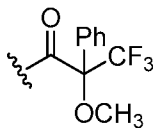


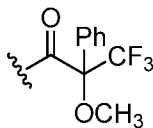
(I)

or pharmaceutically acceptable derivative thereof;

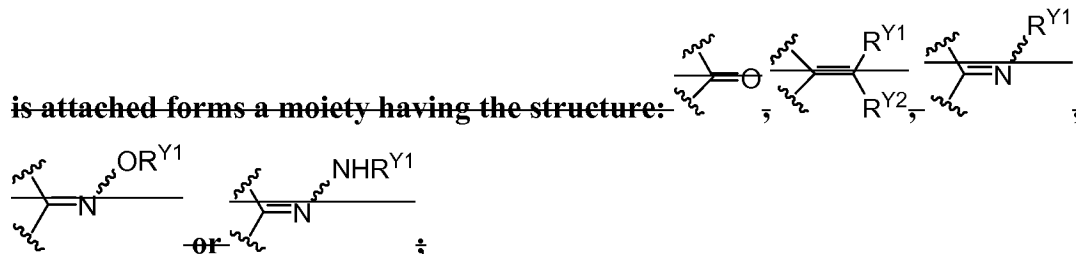
wherein **R₁** and **R₂** are each independently hydrogen, or lower alkyl;

R₃ is hydrogen, substituted or unsubstituted lower alkyl an aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl moiety; or a prodrug moiety or an oxygen protecting group;



R₄ is halogen, -OR^{4A}, oxo, -OC(=O)R^{4A},  or -NR^{4A}R^{4B}; wherein R^{4A} and R^{4B} are independently hydrogen, lower alkyl or lower alkoxy; heteroaliphatic, a nitrogen protecting group or an oxygen protecting group; ~~or R₄, taken together with the carbon atom to which it~~

~~is attached forms a moiety having the structure:~~



R₅ is hydrogen, or lower alkyl;

R₆ is ~~hydrogen, halogen, -CN, -S(O)₁₋₂R^{6A}, -NO₂, -COR^{6A}, -CO₂R^{6A}, -NR^{6A}C(=O)R^{6B}, -NR^{6A}C(=O)OR^{6B}, -CONR^{6A}R^{6B}, substituted or unsubstituted lower alkyl an aliphatic,~~

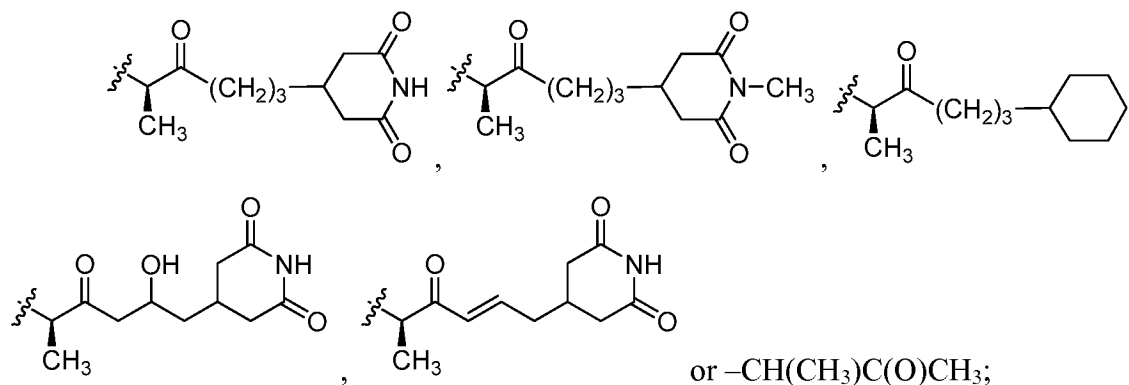
~~heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl moiety, or WR^{6A} ; wherein W is independently O, S or NR^{6C} , wherein each occurrence of R^{6A} , R^{6B} and R^{6C} is independently hydrogen, or an aliphatic, heteroaliphatic, alicyclic, heteroalicyclic, aryl or heteroaryl moiety; or R_6 and R_e , taken together with the carbon atoms to which they are attached, form an alicyclic, heteroalicyclic, aryl or heteroaryl moiety;~~

R_a and each occurrence of R_b and R_c are independently hydrogen;

n is 3;

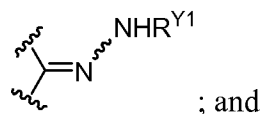
X_1 is O, NR^{X1} or $\text{CR}^{\text{X1}}\text{R}^{\text{X2}}$; wherein R^{X1} and R^{X2} are independently hydrogen;

Q is hydrogen, lower alkyl,

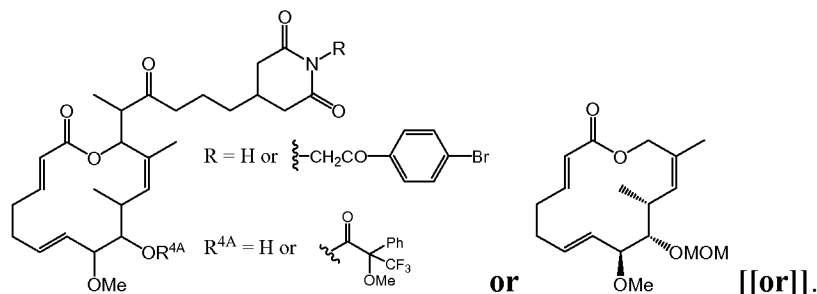


Y_1 and Y_2 are independently hydrogen, lower alkyl, or CF_3 ; or WR^{Y1} ; wherein W is independently -O-, or NR^{Y2} -, wherein each occurrence of R^{Y1} and R^{Y2} is independently hydrogen, or lower alkyl; heteroaliphatic; -or Y_1 and Y_2 together with the carbon atom to which

they are attached form a moiety having the structure:



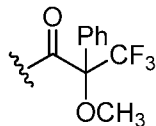
with the proviso that the compound does not have one of the following structures:



2. (CURRENTLY AMENDED) The compound of claim 1, wherein:

R₁ and **R₂** are each independently hydrogen or substituted or unsubstituted lower alkyl;

R₃ is hydrogen, or substituted or unsubstituted lower alkyl or aryl; a prodrug moiety or an oxygen protecting group;



R₄ is halogen, -OR^{4A}, -OC(=O)R^{4A}, oxo, or -NR^{4A}R^{4B}; wherein R^{4A} and R^{4B} are independently hydrogen, or substituted or unsubstituted lower alkyl or lower alkoxy; a nitrogen protecting group or an oxygen protecting group;

R₅ is hydrogen or lower alkyl;

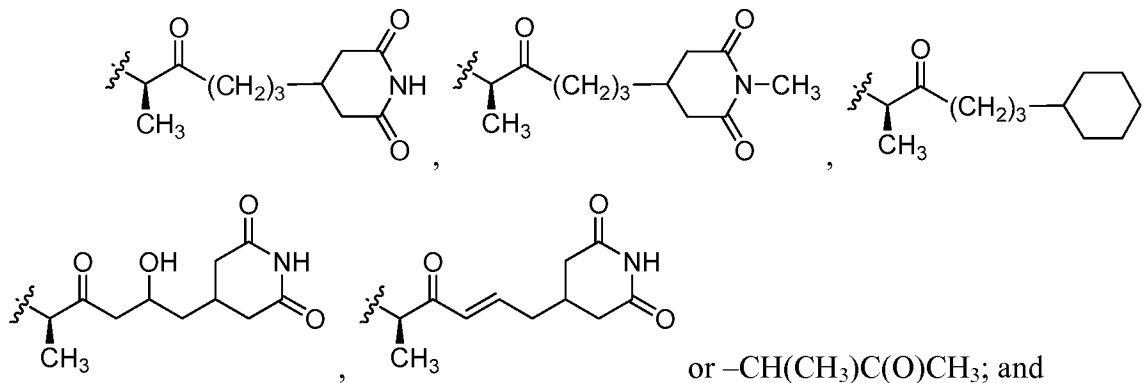
R₆ is ~~hydrogen or~~ substituted or unsubstituted lower alkyl; ~~or **R₆** and **R₆**, taken together with the carbon atoms to which they are attached, form an epoxide, an aziridine or a substituted or unsubstituted cyclopropyl moiety;~~

R_a and each occurrence of **R_b** and **R_c** are independently hydrogen;

n is 3 ;

X₁ is O, NR^{X1} or CR^{X1}R^{X2}; wherein R^{X1} and R^{X2} are independently hydrogen;

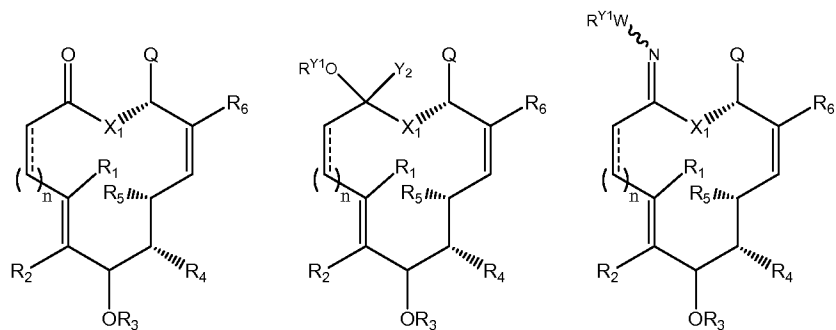
Q is hydrogen, lower alkyl,



Y₁ and **Y₂** are independently hydrogen, lower alkyl, or CF₃; or -WR^{Y1}; wherein W is independently -O-, or -NR^{Y2}-, wherein each occurrence of R^{Y1} and R^{Y2} is independently hydrogen, or an alkyl, or **Y₁** and **Y₂** together with the carbon atom to which they are attached

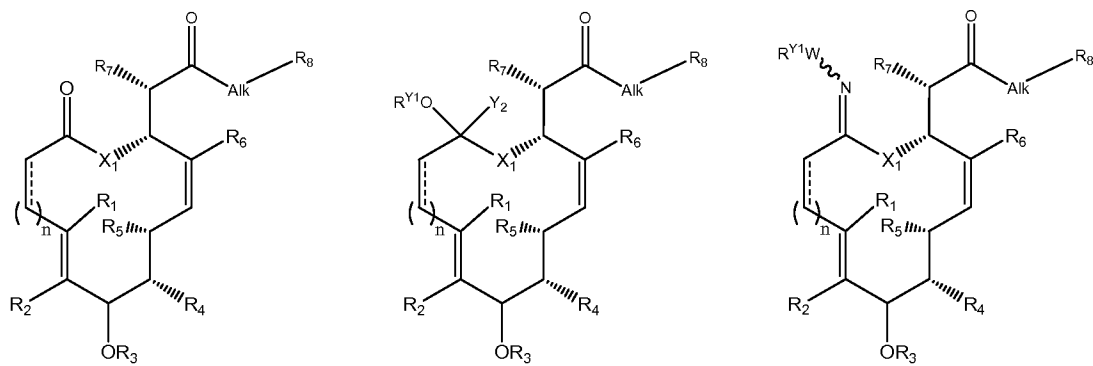
form a moiety having the structure:

3. (PREVIOUSLY PRESENTED) The compound of claim 2, wherein R_a , R_b and R_c are each hydrogen, and the compound has one of the following structures:



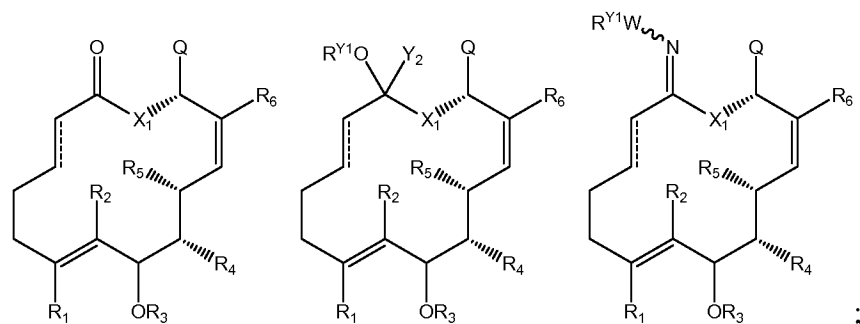
wherein R_1 - R_6 , Y_2 , X_1 , n and Q are as defined in claim 2; W is O or NH; and R^{Y1} is hydrogen, an aliphatic moiety, or a heteroaliphatic moiety.

4.3. (PREVIOUSLY PRESENTED) The compound of claim 2, wherein R_a , R_b and R_c are each hydrogen, Q is a carbonyl-containing moiety and the compound has one of the following structures:



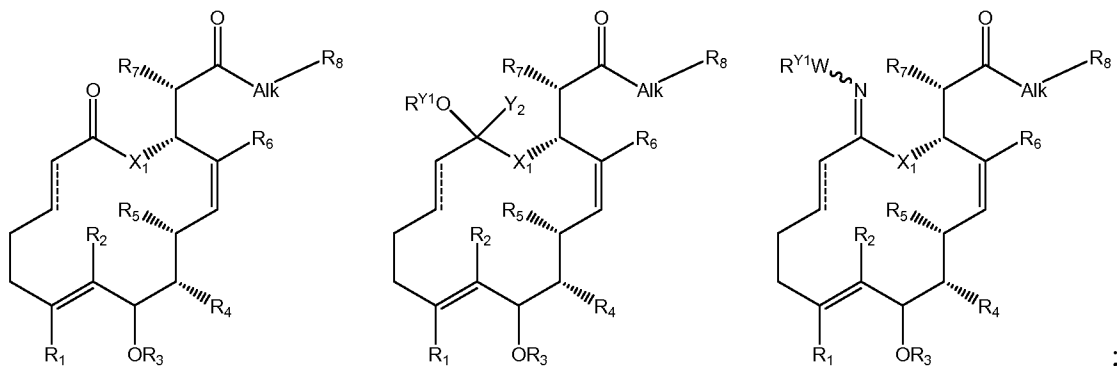
wherein R_1 - R_6 , Y_2 , X_1 , and n are as defined in claim 2; W is O or NH; and R^{Y1} is hydrogen, or an aliphatic, heteroaliphatic; R_7 is a substituted or unsubstituted lower alkyl or heteroalkyl moiety; R_8 is a substituted or unsubstituted alkyl, heteroalkyl, cycloalkyl, heterocycloalkyl; and Alk is a substituted or unsubstituted C_{0-6} alkylenyl or a C_{0-6} alkenylenyl chain wherein up to two non-adjacent methylene units are independently optionally replaced by CO, -O-, or NR^{Z1} ; wherein R^{Z1} is independently hydrogen, or alkyl.

5.4. (PREVIOUSLY PRESENTED) The compound of claim 2, wherein R_a , R_b and R_c are each hydrogen, n is 3 and the compound has one of the following structures:



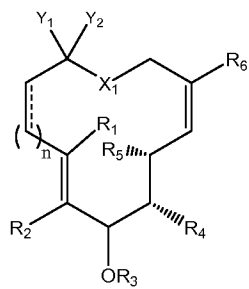
wherein R_1 - R_6 , Y_2 , Q and X_1 are as defined in claim 1; W is O or NH; and R^{Y1} is hydrogen, an aliphatic moiety, or a heteroaliphatic moiety.

6.5. (CURRENTLY AMENDED) The compound of claim 2, wherein R_a , R_b and R_c are each hydrogen, n is 3, Q is a carbonyl-containing moiety, and the compound has one of the following structures:



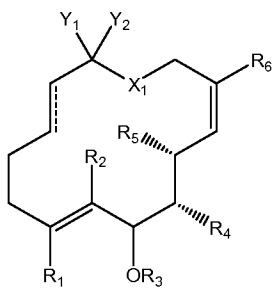
wherein R_1 - R_6 , X_1 and Y_2 are as defined in claim 2; W is O or NH; R^{Y1} is hydrogen, an aliphatic moiety, or a heteroaliphatic moiety; R_7 is a substituted or unsubstituted lower alkyl or heteroalkyl moiety; R_8 is a substituted or unsubstituted alkyl, heteroalkyl, cycloalkyl, heterocycloalkyl; and Alk is a substituted or unsubstituted C_{0-6} alkylene or C_{0-6} alkenylene chain wherein up to two non-adjacent methylene units are independently optionally replaced by CO, NR^{Z1} ; wherein R^{Z1} is independently hydrogen, or alkyl, and R_8 is a substituted or unsubstituted alkyl, heteroalkyl, cycloalkyl, or a heterocycloalkyl moiety.

7.6: (ORIGINAL) The compound of claim 2, wherein R_a, R_b and R_c are each hydrogen, Q is hydrogen, and the compound has the following structure:



wherein R₁-R₆, n, X₁, Y₁ and Y₂ are as defined in claim 2.

8.7: (ORIGINAL) The compound of claim 2, wherein R_a, R_b and R_c are each hydrogen, n is 3, Q is hydrogen, and the compound has the following structure:



wherein R₁-R₆, X₁, Y₁ and Y₂ are as defined in claim 2.

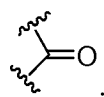
9.8: (PREVIOUSLY PRESENTED) The compound of claim 1, wherein R₁ and R₂ are each hydrogen.

10.9: (PREVIOUSLY PRESENTED) The compound of claim 1, wherein R₅ and R₆ are each methyl.

11.10: (PREVIOUSLY PRESENTED) The compound of claim 1, wherein R₃ is lower alkyl.

12.11: (PREVIOUSLY PRESENTED) The compound of claim 11, wherein R₃ is methyl.

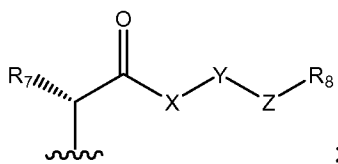
13. 12. (PREVIOUSLY PRESENTED) The compound of claim 1, wherein R₄ is OH, OAc, NH₂ or halogen, or R₄ taken together with the carbon atom to which it is attached forms a moiety having

the structure: .

14. 13. (ORIGINAL) The compound of claim 4 or 6, wherein R₇ is lower alkyl.

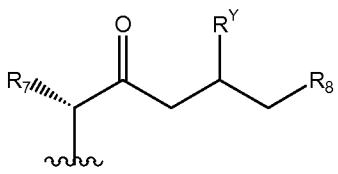
15. 14. (ORIGINAL) The compound of claim 14, wherein R₇ is methyl.

16. 15. (PREVIOUSLY PRESENTED) The compound of claim 1, wherein Q has the structure:



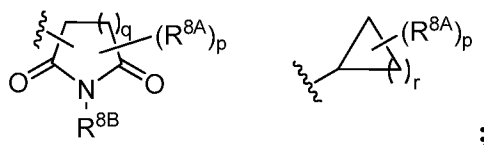
wherein R₇ is a substituted or unsubstituted, lower alkyl moiety; R₈ is a substituted or unsubstituted carbocyclic or heterocyclic moiety; and X, Y and Z are independently a bond, -O-, -C(=O)-, -NR^{Z1}-, -CHOR^{Z1}; or a substituted or unsubstituted C₀₋₆ alkylene or C₀₋₆ alkenylene wherein up to two non-adjacent methylene units are independently optionally replaced by CO, O, -or NR^{Z1}; wherein R^{Z1} is hydrogen or alkyl; and pharmaceutically acceptable derivatives thereof.

17. 16. (PREVIOUSLY PRESENTED) The compound of claim 16, wherein Q has the structure:



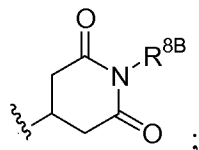
wherein R₇ is a substituted or unsubstituted lower alkyl moiety; R₈ is a substituted or unsubstituted carbocyclic moiety, or a heterocyclic moiety; and R^Y is hydrogen, -OR^{Y1}; wherein R^{Y1} is hydrogen, alkyl, or heteroalkyl.

18. ~~17.~~ (PREVIOUSLY PRESENTED) The compound of claim 4, wherein R_8 is one of:



wherein p is an integer from 0 to 5; q is 1 or 2, r is an integer from 1 to 6; each occurrence of R^{8A} is independently hydrogen; and each occurrence of R^{8B} is independently hydrogen or lower alkyl.

19. ~~18.~~ (ORIGINAL) The compound of claim 18, wherein R_8 has the structure:



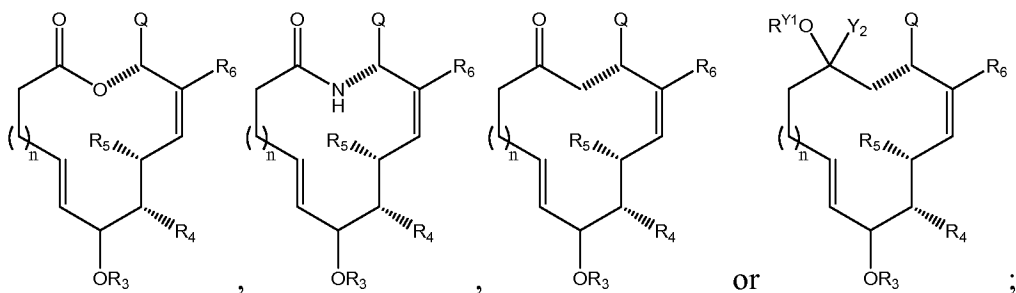
wherein R^{8B} is hydrogen or lower alkyl.

20. ~~19.~~ (PREVIOUSLY CANCELED).

21. ~~20.~~ (PREVIOUSLY PRESENTED) The compound of claim 3, wherein Y_1 is OR^{Y1} and Y_2 is lower alkyl or CF_3 ; wherein R^{Y1} is hydrogen or lower alkyl.

22. ~~21.~~ (ORIGINAL) The compound of claim 21, wherein Y_1 is OH and Y_2 is CF_3 .

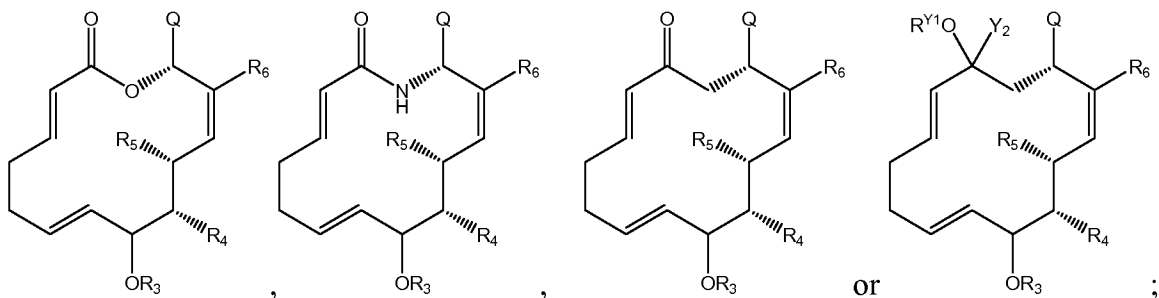
23. 22. (ORIGINAL) The compound of claim 2 wherein R_a , R_b and R_c are each hydrogen, and the compound has one of the structures:



or pharmaceutically acceptable derivative thereof;

wherein R_3 - R_6 , n and Q are as defined in claim 2; and Y_2 and R^{Y1} are independently hydrogen or lower alkyl.

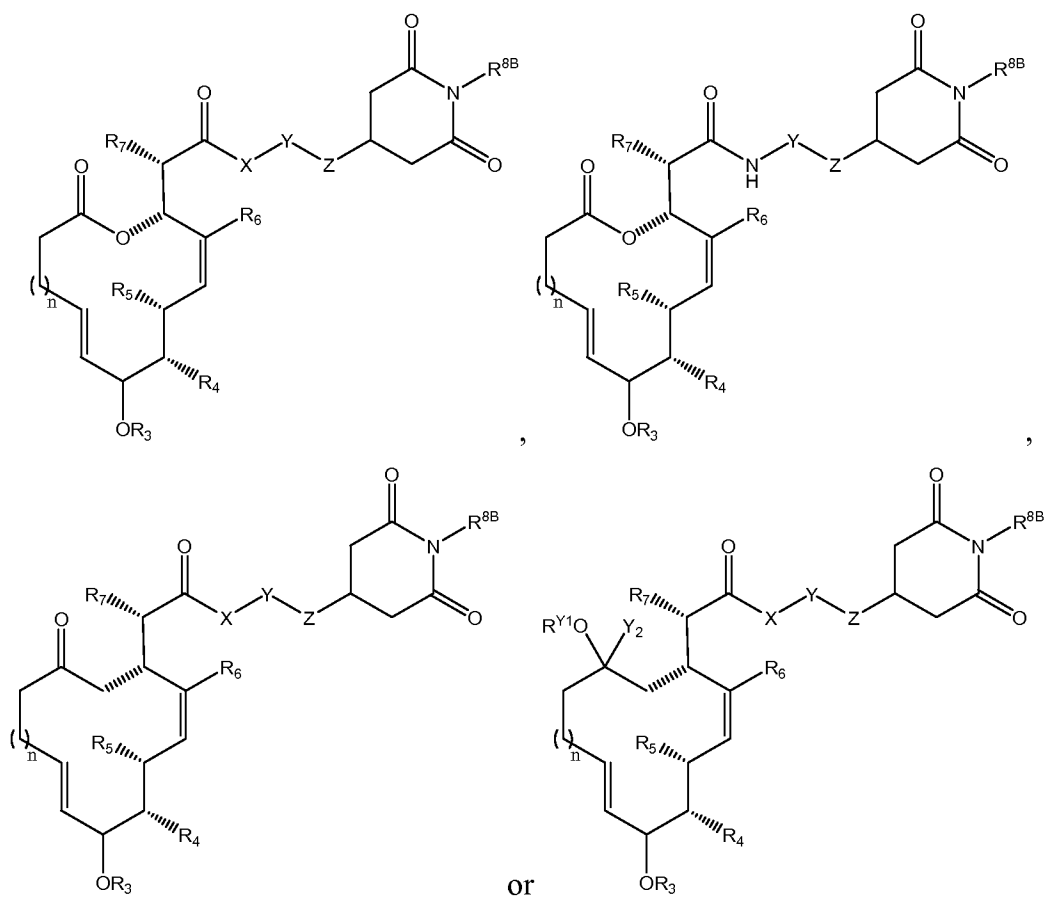
24. 23. (ORIGINAL) The compound of claim 2 wherein the compound has the structure:



or pharmaceutically acceptable derivative thereof;

wherein R_3 - R_6 and Q are as defined in claim 2; and Y_2 and R^{Y1} are independently hydrogen or lower alkyl.

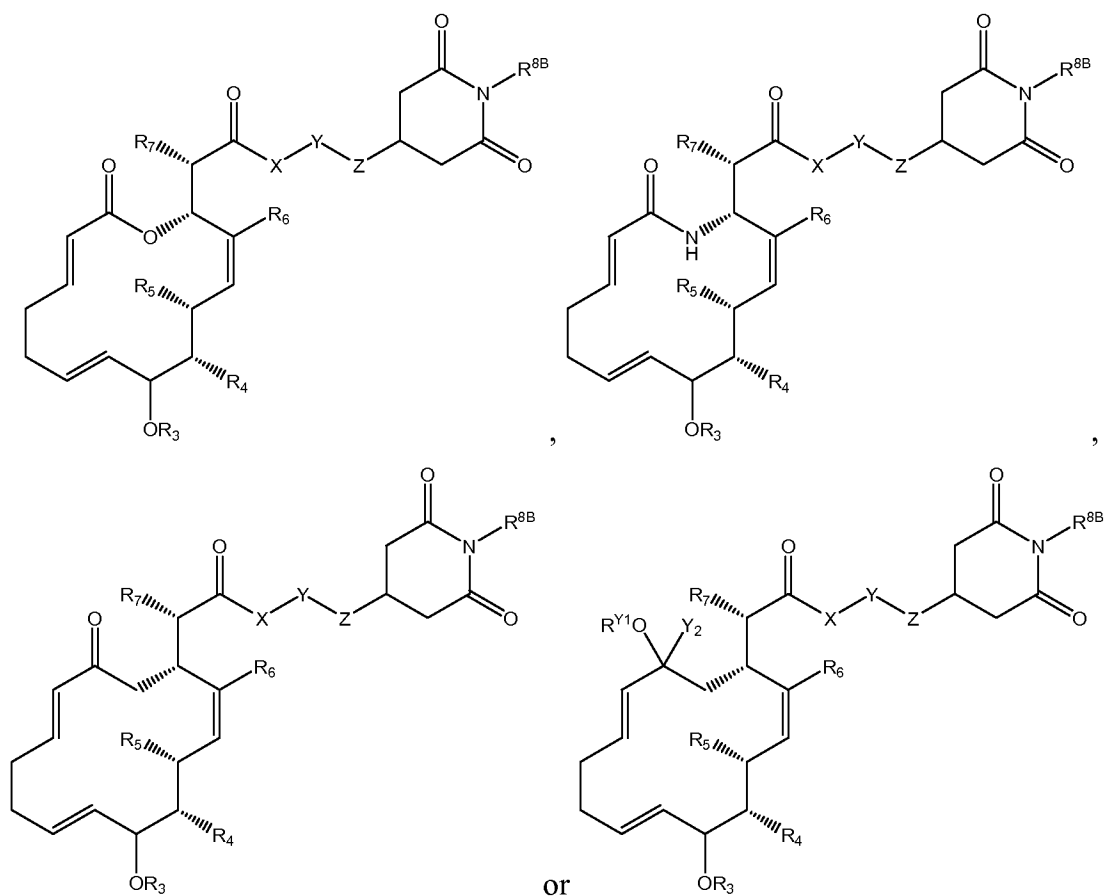
25. 24. (PREVIOUSLY PRESENTED) The compound of claim 2 wherein the compound has the structure:



or pharmaceutically acceptable derivative thereof;

wherein R_3 - R_6 and n are as defined in claim 2; Y_2 and R^{Y1} are independently hydrogen or lower alkyl; R_7 is a substituted or unsubstituted, lower alkyl moiety; R^{8B} is hydrogen or lower alkyl; and X , Y and Z are independently a bond, $-O-$, $-C(=O)-$, $-NR^{Z1}-$, $-CHOR^{Z1}$; or a substituted or unsubstituted C_{0-6} alkylene or C_{0-6} alkenylene chain wherein up to two non-adjacent methylene units are independently optionally replaced by CO , O , or NR^{Z1} ; and R^{Z1} is hydrogen, or alkyl.

26. 25. (PREVIOUSLY PRESENTED) The compound of claim 2 wherein the compound has the structure:

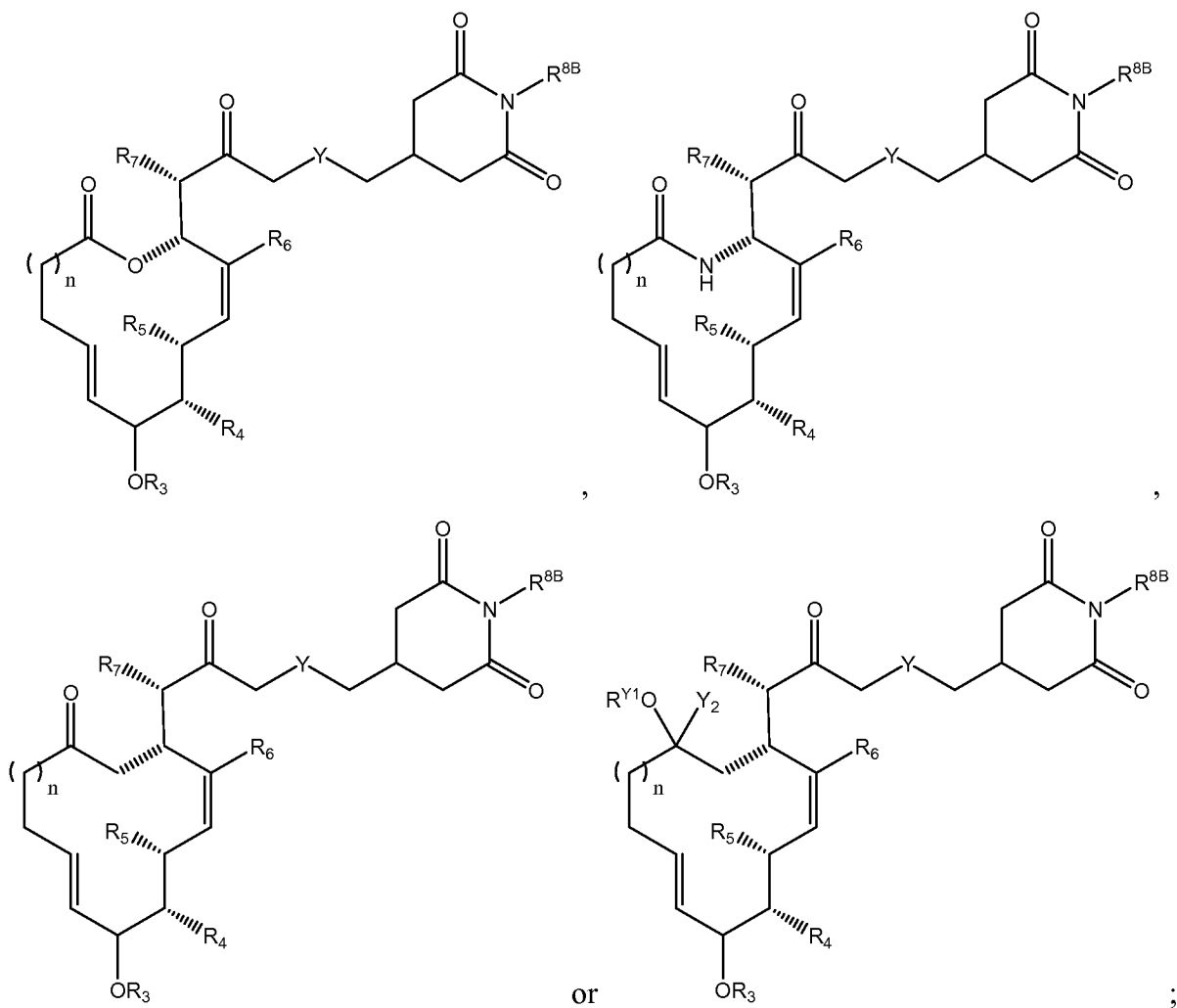


or pharmaceutically acceptable derivative thereof;

wherein R_3 - R_6 are as defined in claim 2; Y_2 and R^{Y1} are independently hydrogen or lower alkyl; R_7 is a substituted or unsubstituted, lower alkyl moiety; R^{8B} is hydrogen or lower alkyl; and X, Y and Z are independently a bond, -O-, -C(=O)-, -NR^{Z1}-, or -CHOR^{Z1}-; or a substituted or unsubstituted C₀₋₆ alkylenyl or C₀₋₆ alkenylenyl chain wherein up to two non-adjacent methylene units are independently optionally replaced by CO, O, or NR^{Z1}; and R^{Z1} is hydrogen or alkyl.

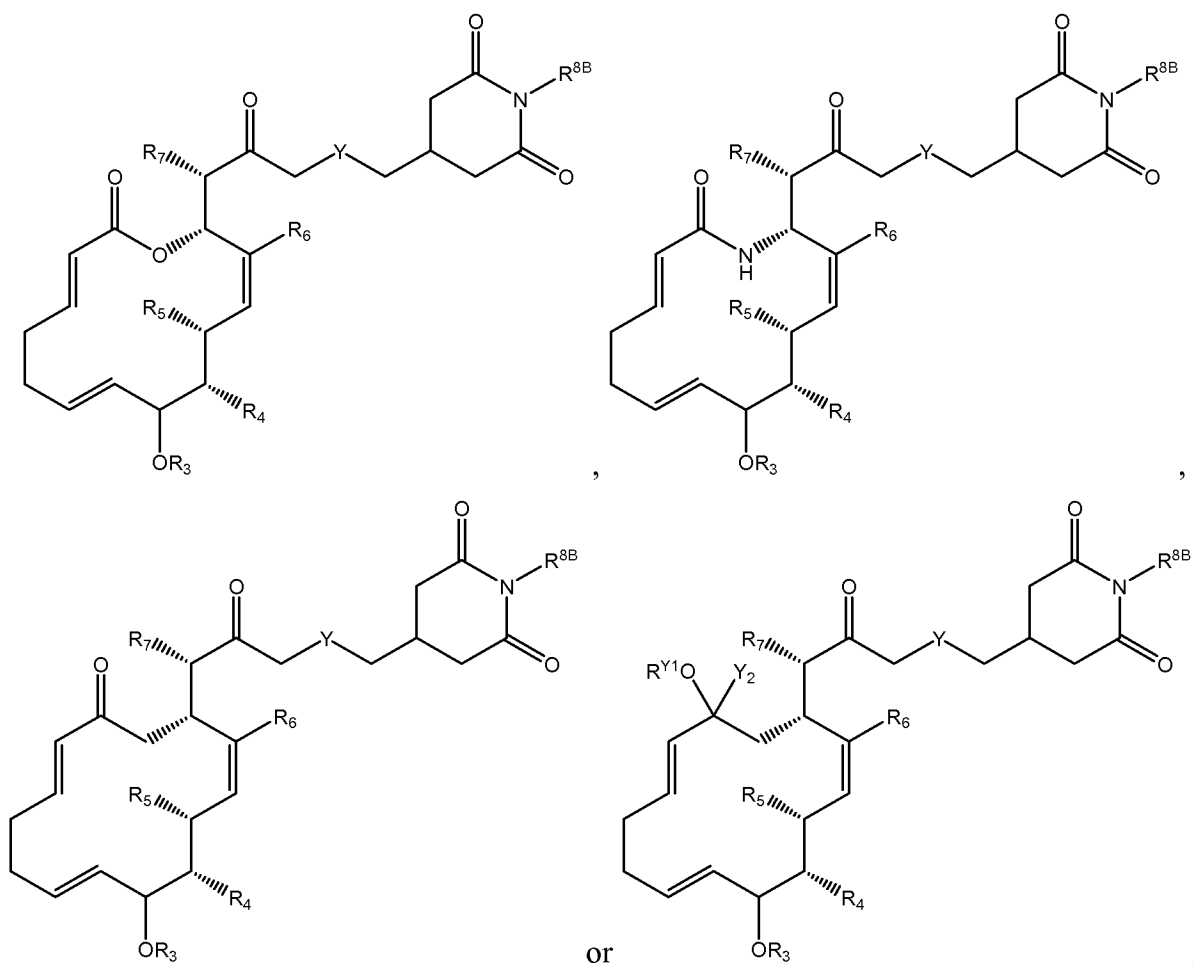
27. 26. (PREVIOUSLY PRESENTED) The compound of claim 25 or 26, wherein -X-Y-Z together represents the moiety -CH₂-Y-CH₂-; wherein Y is -CHOR^{Y1} or C=O; and R^{Y1} and R^{Y2} are independently hydrogen or alkyl.

28. 27. (PREVIOUSLY PRESENTED) The compound of claim 2 wherein the compound has the structure:



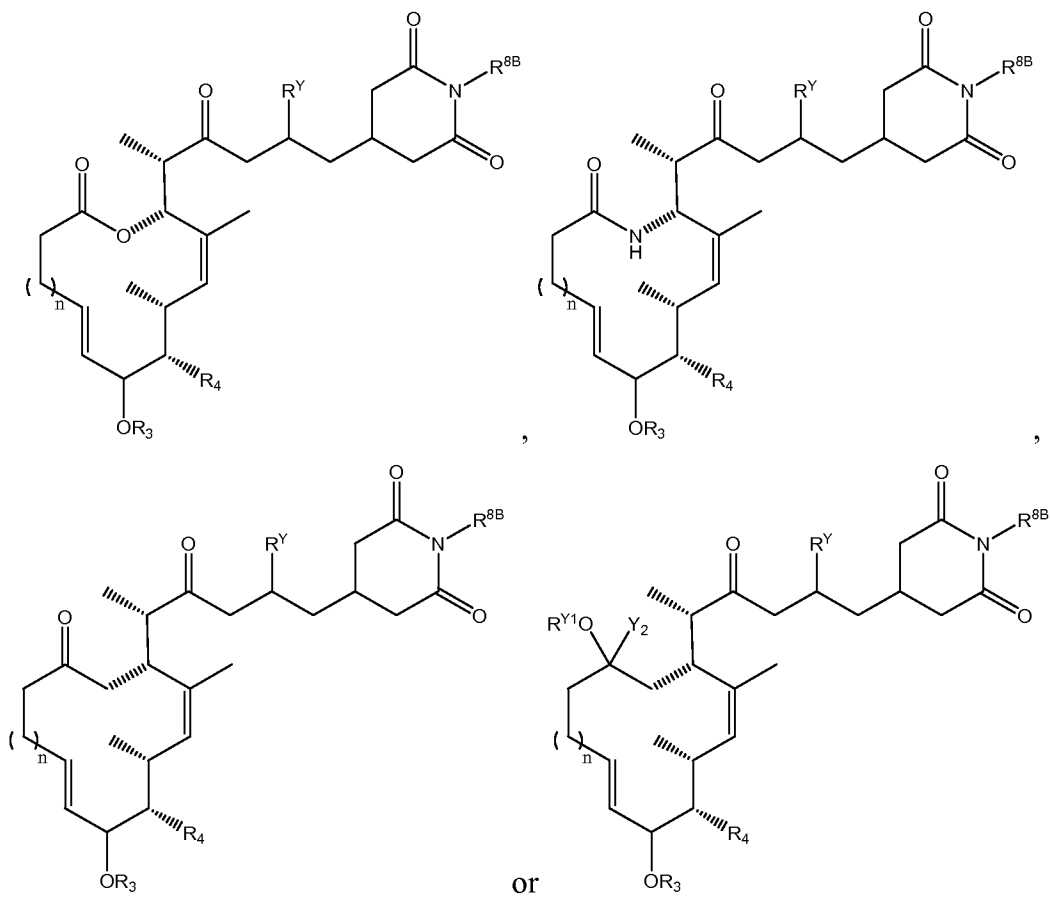
wherein R_3 - R_6 and n are as defined in claim 2; Y_2 and R^{Y1} are independently hydrogen or lower alkyl; R_7 is a substituted or unsubstituted, lower alkyl moiety; R^{8B} is hydrogen or lower alkyl; and Y is $-CHOR^{Y1}$ or $C=O$; and R^{Y1} is hydrogen, alkyl, or heteroalkyl.

29. 28. (PREVIOUSLY PRESENTED) The compound of claim 2 wherein the compound has the structure:



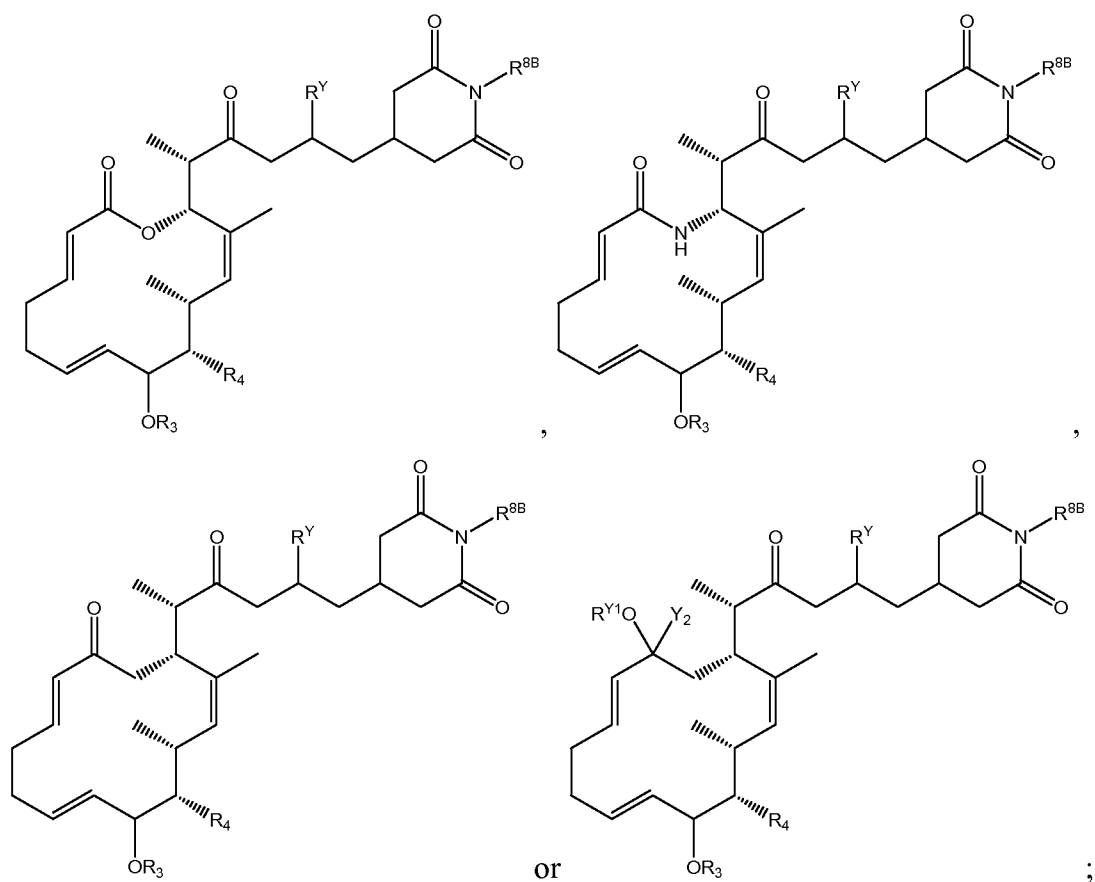
wherein R_3 - R_6 are as defined in claim 2; Y_2 and R^{Y1} are independently hydrogen or lower alkyl; R_7 is a substituted or unsubstituted, lower alkyl moiety; R^{8B} is hydrogen or lower alkyl; and Y is $-\text{CHOR}^{Y1}$, or C=O ; and R^{Y1} is hydrogen, alkyl, or heteroalkyl.

30.29. (PREVIOUSLY PRESENTED) The compound of claim 2 wherein the compound has the structure:



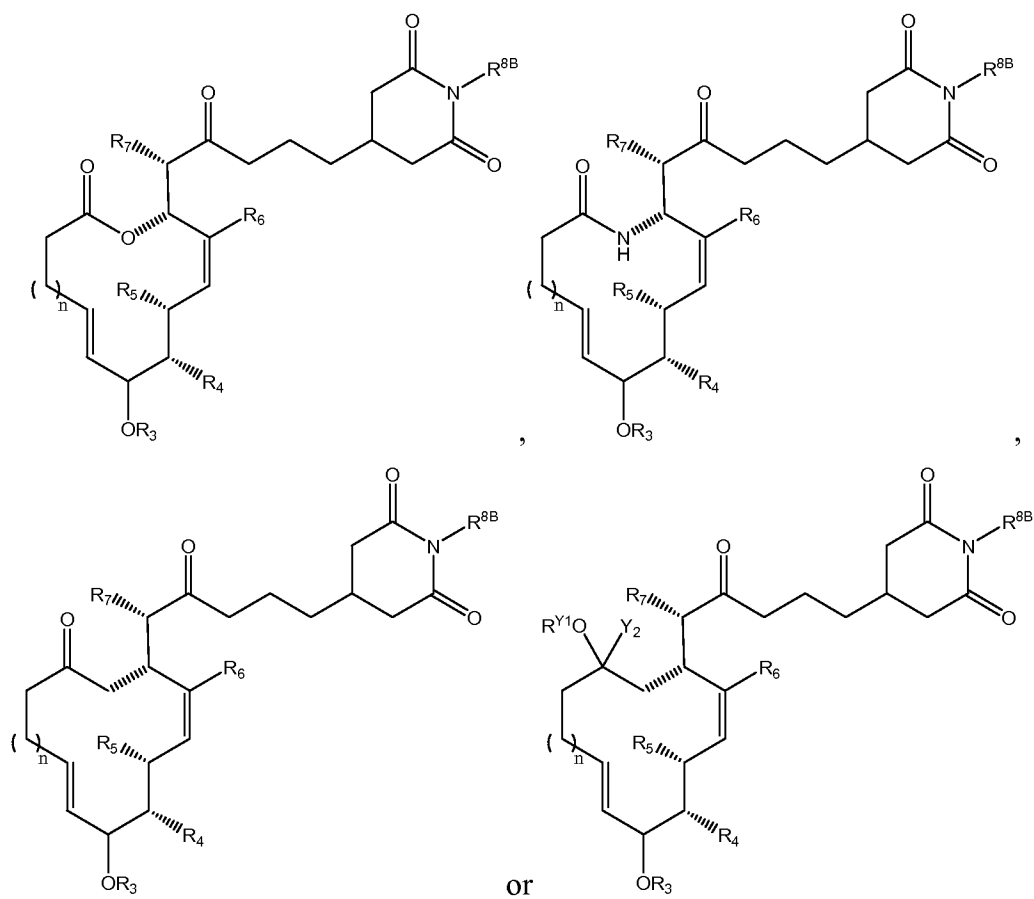
wherein n , R_3 and R_4 are as defined in claim 2; Y_2 and R^{Y1} are independently hydrogen or lower alkyl; R^{8B} is hydrogen or lower alkyl; and R^Y is hydrogen, or $-OR^{Y1}$; wherein R^{Y1} is hydrogen, alkyl, or heteroalkyl.

31.30. (PREVIOUSLY PRESENTED) The compound of claim 2 wherein the compound has the structure:



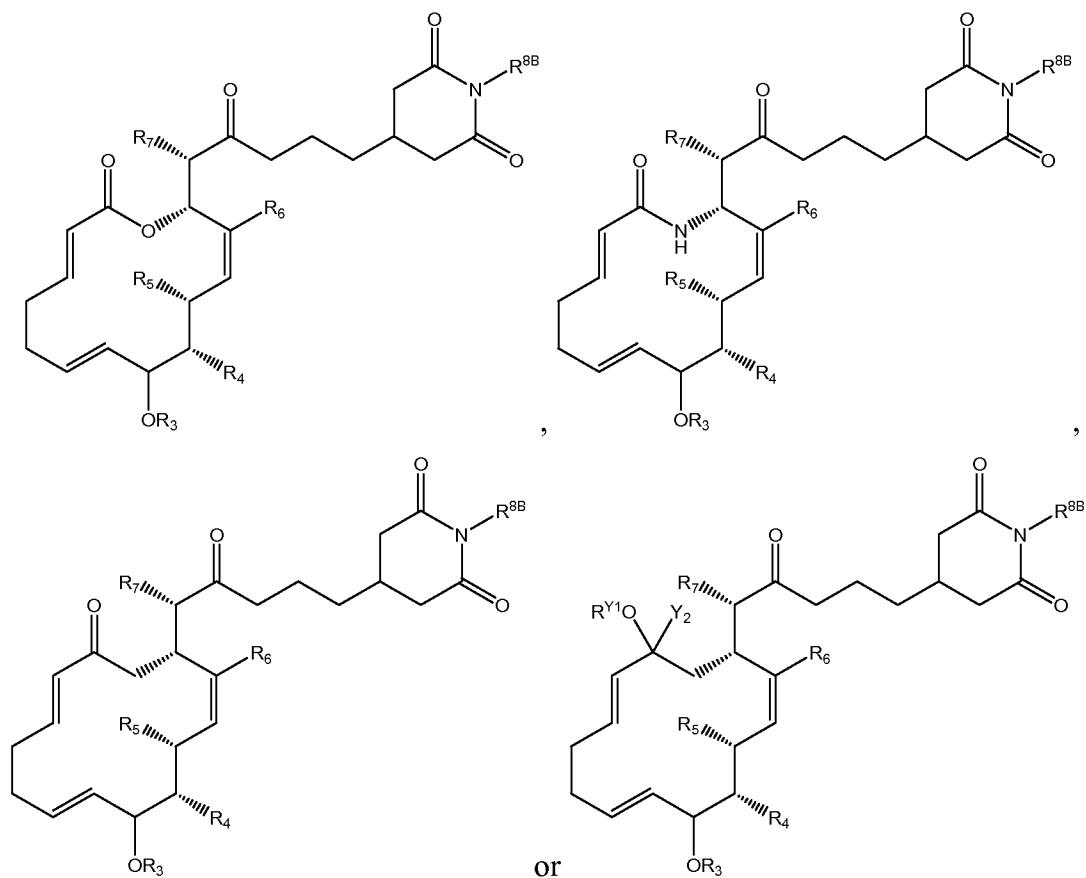
wherein R_3 and R_4 are as defined in claim 2; Y_2 and R^{Y1} are independently hydrogen or lower alkyl; R^{8B} is hydrogen or lower alkyl; and R^Y is hydrogen, or $-OR^{Y1}$; wherein R^{Y1} is hydrogen, alkyl, or heteroalkyl.

32. 34. (PREVIOUSLY PRESENTED) The compound of claim 2 wherein the compound has the structure:



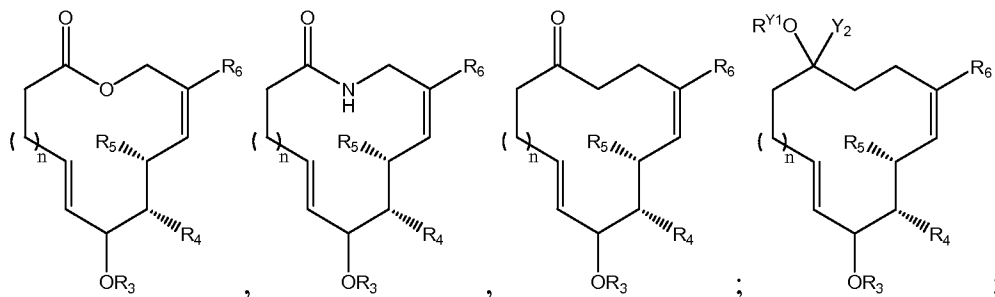
wherein R_3 - R_6 and n are as defined in claim 11; Y_2 and R^{Y1} are independently hydrogen or lower alkyl; R_7 is a substituted or unsubstituted, lower alkyl moiety; and R^{8B} is hydrogen or lower alkyl.

33. **(PREVIOUSLY PRESENTED)** The compound of claim 2 wherein the compound has the structure:



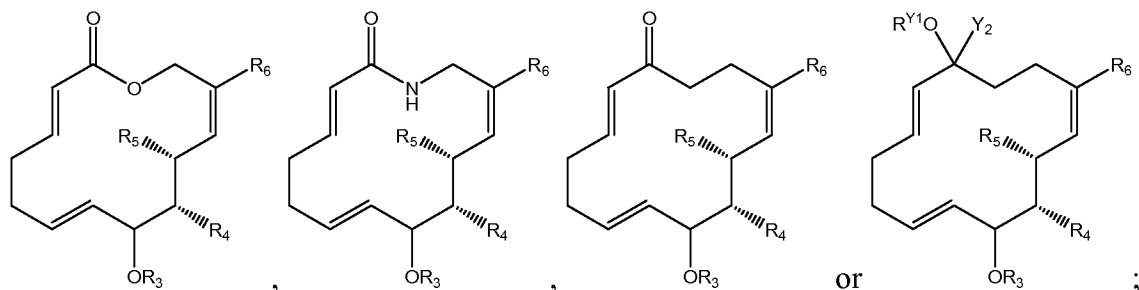
wherein R_3 - R_6 are as defined in claim 11; Y_2 and R^{Y1} are independently hydrogen or lower alkyl; R_7 is a substituted or unsubstituted, lower alkyl moiety; and R^{8B} is hydrogen or lower alkyl.

34. **(ORIGINAL)** The compound of claim 2 wherein the compound has the structure:



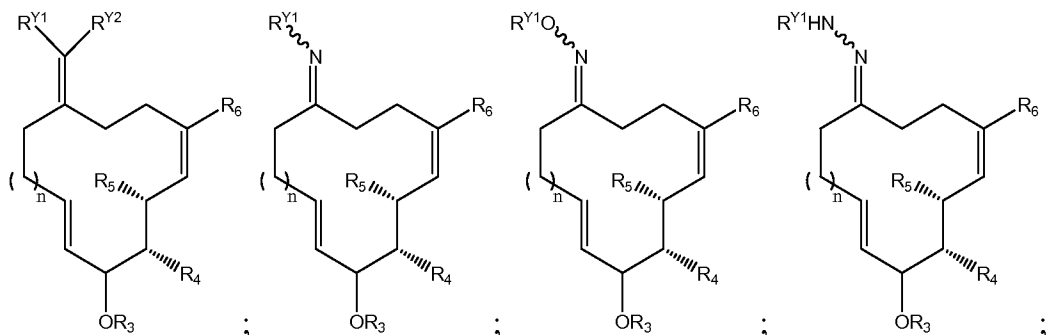
wherein R_3 - R_6 and n are as defined in claim 2; and Y_2 and R^{Y1} are independently hydrogen or lower alkyl.

35. **(ORIGINAL)** The compound of claim 2 wherein the compound has the structure:



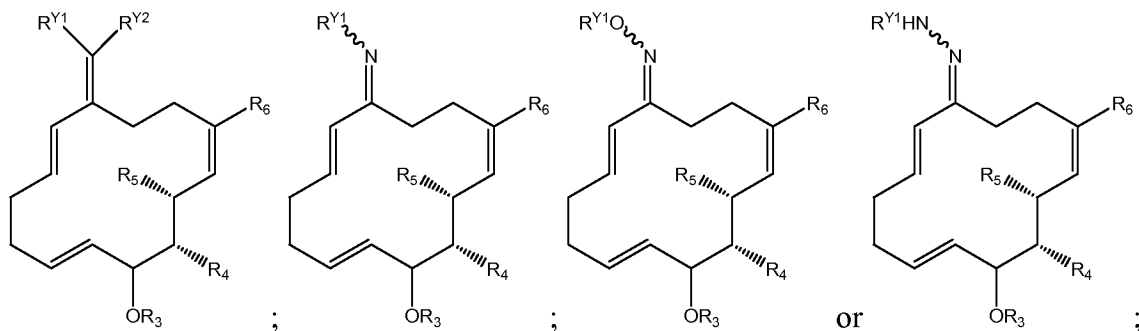
wherein R₃-R₆ are as defined in claim 2; and Y₂ and R^{Y1} are independently hydrogen or lower alkyl.

36. **(ORIGINAL)** The compound of claim 2 wherein the compound has the structure:



wherein R₃-R₆ and n are as defined in claim 2; and Y₂ and R^{Y1} are independently hydrogen or lower alkyl.


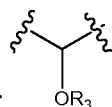
37. **(ORIGINAL)** The compound of claim 2 wherein the compound has the structure:

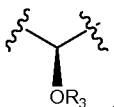


wherein R₃-R₆ are as defined in claim 2; and Y₂ and R^{Y1} are independently hydrogen or lower alkyl.

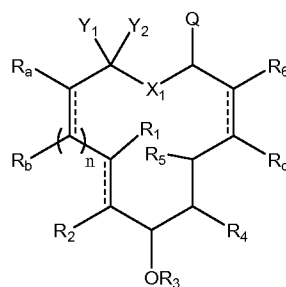
Claims 38-47 (**PREVIOUSLY CANCELED**).

48. (**PREVIOUSLY PRESENTED**) The compound of claim 35, wherein Y_2 is lower alkyl optionally substituted with one to three halogen atoms and R^{Y1} is hydrogen or lower alkyl; R_3 , R_5 and R_6 are each methyl; R_4 is OH, OAc, NH_2 or F, or R_4 taken together with the carbon atom to

which it is attached forms a moiety having the structure: ; and the stereocenter 

has the following stereochemistry .

49. (**CURRENTLY AMENDED**) A pharmaceutical composition comprising:
a pharmaceutically acceptable carrier, adjuvant or vehicle; and
a compound having the structure:

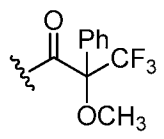


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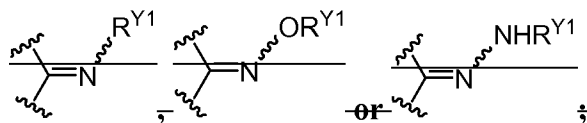
or pharmaceutically acceptable salt thereof;

wherein R_1 and R_2 are each independently hydrogen or lower alkyl;

R_3 is hydrogen or substituted or unsubstituted lower alkyl ~~lower alkyl~~;

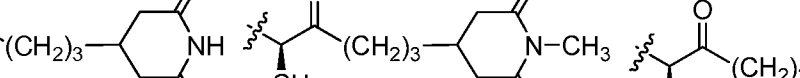
R_4 is hydrogen, halogen, $-OR^{4A}$, oxo, $-OC(=O)R^{4A}$,  or $-NR^{4A}R^{4B}$; wherein R^{4A} and R^{4B} are independently hydrogen, lower alkyl or lower alkoxy; heteroaliphatic, a nitrogen protecting group or an oxygen protecting group; ~~or R_4 , taken together with the~~

The reaction scheme shows a carbenoid intermediate on the left, represented as a carbon atom double-bonded to an oxygen atom with a negative charge (C=O⁻). This intermediate is in equilibrium with a substituted alkene on the right. The alkene has a double bond between two carbon atoms. The left carbon is bonded to two wavy lines, representing generic substituents. The right carbon is bonded to two groups, R^{Y1} and R^{Y2}, and is also bonded to a wavy line. The equilibrium is indicated by a double-headed arrow.

~~$$\text{R}_6 \text{ is hydrogen, halogen, CN, S(O)}_{1-2}\text{R}^{6A}, \text{NO}_2, \text{COR}^{6A}, \text{CO}_2\text{R}^{6A}, \text{NR}^{6A}\text{C(=O)R}^{6B},$$~~

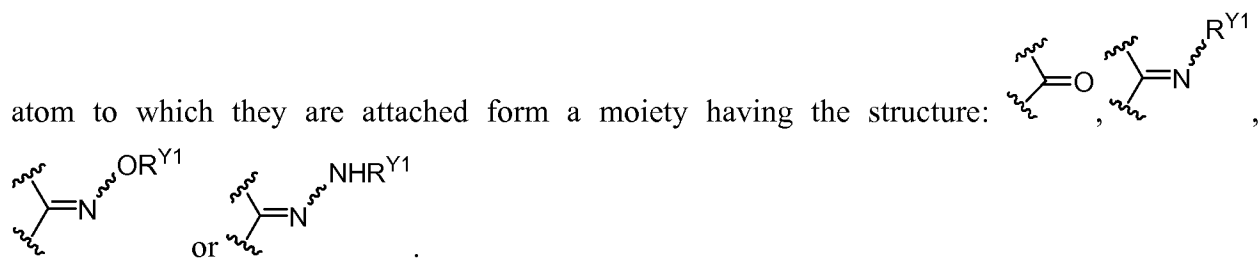
R_a and each occurrence of **R_b** and **R_c** are independently hydrogen;

X₁ is O, NR^{X₁} or CR^{X₁}R^{X₂}; wherein R^{X₁} and R^{X₂} are independently hydrogen;



 or $-\text{CH}(\text{CH}_3)\text{C}(\text{O})\text{CH}_3$; and

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50. **(ORIGINAL)** The pharmaceutical composition of claim 49 wherein the compound is present in an amount effective to inhibit the metastasis of tumor cells.

51. **(ORIGINAL)** The pharmaceutical composition of claim 49 wherein the compound is present in an amount effective to inhibit angiogenesis.

52. **(ORIGINAL)** The composition of claim 49, further comprising a cytotoxic agent.

53. **(ORIGINAL)** The composition of claim 52, wherein the cytotoxic agent is an anticancer agent.

54. **(ORIGINAL)** The composition of claim 53, wherein the anticancer agent is 12,13-desoxyepothilone B, (E)-9,10-dehydro-12,13-desoxyEpoB, 26-CF3-(E)-9,10-dehydro-12,13-desoxyEpoB, taxol, radicicol or TMC-95A/B.

55. **(ORIGINAL)** The composition of claim 49, further comprising a palliative agent.

56. **(ORIGINAL)** A method for treating or lessening the severity of metastasis of tumor cells in a subject comprising:

administering to a subject in need thereof a therapeutically effective amount of a composition according to claim 49;

said method optionally further comprising a cytotoxic agent.

57. **(ORIGINAL)** The method of claim 56, wherein the method is used to treat or lessen the severity of metastasis of prostate, breast, colon, bladder, cervical, skin, testicular, kidney,

ovarian, stomach, brain, liver, pancreatic or esophageal cancer or lymphoma, leukemia, or multiple myeloma.

58. **(ORIGINAL)** The method of claim 57, wherein the cancer is a solid tumor.

59. **(ORIGINAL)** The method of claim 56, wherein the cytotoxic agent is an anticancer agent.

60. **(ORIGINAL)** The method of claim 59, wherein the anticancer agent is 12,13-desoxyepothilone B, (E)-9,10-dehydro-12,13-desoxyEpoB, 26-CF3-(E)-9,10-dehydro-12,13-desoxyEpoB, taxol, radicicol or TMC-95A/B.

61. **(ORIGINAL)** The method of claim 59, further comprising administering a palliative agent.

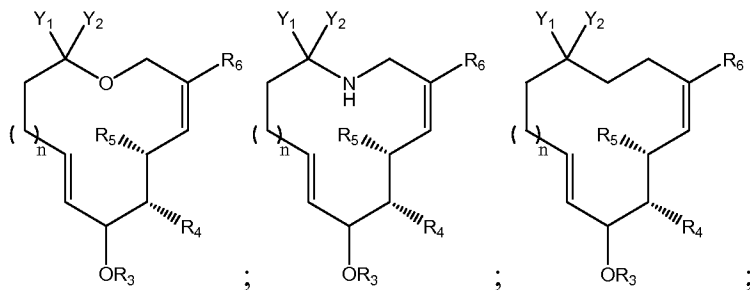
62. **(ORIGINAL)** A method for inhibiting angiogenesis in a subject comprising:
administering to a subject in need thereof an angiogenesis inhibiting amount of a composition according to claim 49.

63. **(ORIGINAL)** The method of claim 62, wherein the angiogenesis causes an angiogenesis dependent disease.

64. **(ORIGINAL)** The method of claim 63, wherein the angiogenesis dependent disease is ocular angiogenic diseases, diabetic retinopathy, retinopathy of prematurity, corneal graft rejection, neovascular glaucoma, retrolental fibroplasias, rubeosis, solid tumors, blood born tumors, leukemias, tumor metastases, benign tumors, acoustic neuromas, neurofibromas, trachomas, pyogenic granulomas, rheumatoid arthritis, psoriasis, Osler-Webber Syndrome, myocardial angiogenesis, plaque neovascularization, telangiectasia, hemophiliac joints, angiofibroma, or wound granulation.

Claims 65-70 **(PREVIOUSLY CANCELED)**

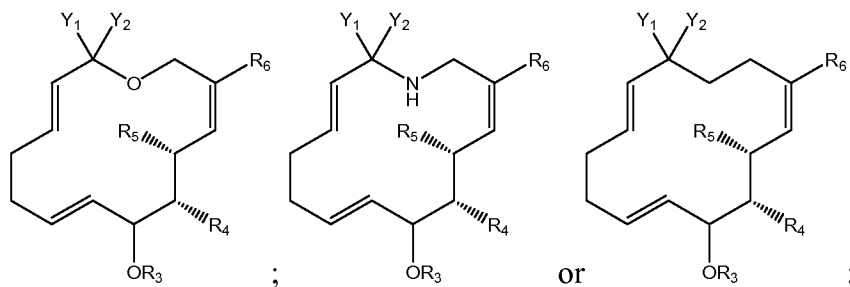
71. **(PREVIOUSLY PRESENTED)** The compound of claim 7 having one of the structure:



wherein Y_1 and Y_2 are independently hydrogen, lower alkyl, or CF_3 ; or $-WR^{Y1}$; wherein W is independently -O-, or $-NR^{Y2}$ -, wherein each occurrence of R^{Y1} and R^{Y2} is independently hydrogen, or an alkyl; or Y_1 and Y_2 together with the carbon atom to which they are attached

form a moiety having the structure: , or .

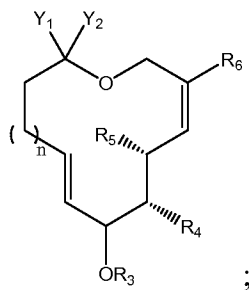
72. **(PREVIOUSLY PRESENTED)** The compound of claim 8 having one of the structure:



wherein Y_1 and Y_2 are independently hydrogen, lower alkyl, or CF_3 ; or $-WR^{Y1}$; wherein W is independently -O-, or $-NR^{Y2}$ -, wherein each occurrence of R^{Y1} and R^{Y2} is independently hydrogen, or an alkyl; or Y_1 and Y_2 together with the carbon atom to which they are attached

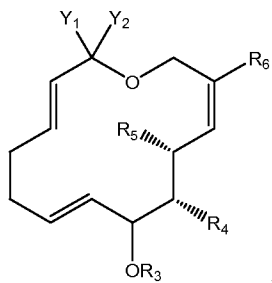
form a moiety having the structure: , or .

73. **(PREVIOUSLY PRESENTED)** The compound of claim 71 having the structure:



wherein n is 3; and **Y**₁ and **Y**₂ are independently hydrogen, lower alkyl, or CF₃.

74. **(PREVIOUSLY PRESENTED)** The compound of claim 72 having the structure:



wherein **Y**₁ and **Y**₂ are independently hydrogen, lower alkyl, or CF₃.

75. **(PREVIOUSLY PRESENTED)** The compound of claim 73 or 74, wherein R₅ and R₆ are each methyl.

76. **(PREVIOUSLY PRESENTED)** The compound of claim 73 or 74, wherein R₃ is lower alkyl.

77. **(PREVIOUSLY PRESENTED)** The compound of claim 76, wherein R₃ is methyl.

78. **(PREVIOUSLY PRESENTED)** The compound of claim 73 or 74, wherein R₄ is OH, OAc, NH₂ or halogen.